## **NWX-HHS FDA (US)**

Moderator: Irene Aihie October 23, 2014 1:00 pm CT

Coordinator:

Welcome and thank you for standing by. All participants are in a listen-only mode for the duration of today's conference which is being recorded. If you have any objections you may disconnect at this time.

After the presentation we will conduct a question and answer session at which time if you have a question please press Star 1 and record your first and last name when prompted.

Your host for today is Ms. Irene Aihie. Thank you. You may begin.

Irene Aihie:

Hello and welcome to today's FDA Webinar. I am Irene Aihie of CDRH's Office of Communication and Education.

Today we will be discussing the draft guidance document titled Framework for Regulatory Oversight of Laboratory Developed Tests also known as LDTs which published on October 3rd of this year.

This draft guidance describes a risk-based framework for addressing the regulatory oversight of a subset of in vitro diagnostic devices or IVDs which are specifically referred to as Laboratory Developed Tests or LDTs.

These products are evaluated in CDRH's Office of In Vitro Diagnostics and Radiological Health also known as OIR.

Today Katherine Serrano, the Deputy Director in OIR's Division of Chemistry and Toxicology Devices will present an overview of the draft guidance document.

After her presentation we will host a Q&A session during which Katherine will be joined by Dr. Alberto Gutierrez, the Director of OIR and Dr. Elizabeth Mansfield of OIR's Personalized Medicine Staff.

Following today's Webinar a slide presentation, audio recording and written transcript will be available on our web site at www.fda.gov/cdrhwebinar. Now I give you Katherine.

Katherine Serrano: Thank you so much. FDA is very happy to be here today to give this

Webinar to you folks. You know, before I get too deep into the meat of this

Webinar I wanted to just provide sort of the purpose and what the scope is for this Webinar today.

So we'd like to provide you with an overview and some context for the proposed oversight framework and also answer any clarifying questions that you may have about the specific proposals we have outlined in this draft guidance document.

Our goal really is to be able to enable you to provide better feedback to the docket that has been created for this guidance document.

And I did want to note that one thing that we aren't able to do today is actually receive comments from you on the draft guidance document.

We need to follow the formal process of having folks submit those comments to the public docket so that they're recorded appropriately.

And then also, you know, in my question and in the question and answer period that will follow the sort of the formal presentation that I will give, again, I'll ask you to sort of hold off on asking comments that go beyond what's in the guidance document.

We can, I can answer clarification questions about what our intention was with what was in - that's proposed in the guidance document-but anything beyond that does need to be submitted to the - as part of the formal comment process.

So just to provide you with an overview of what I would like to get through today is I would like to provide some background for where this - where we're at and how we got here, talk a little bit about our current proposal and then discuss sort of the process and what the next steps are.

So, you know, in 1976 the medical device amendments were made to the Federal Food Drug and Cosmetic Act that gave FDA the authority to regulate all in vitro diagnostic devices as devices which included laboratory tests.

And that is regardless of actually whether they were developed or manufactured by a laboratory or a conventional manufacturer.

Now with that said, FDA has generally used enforcement discretion for laboratory developed tests which we've defined to be tests that are intended

for clinical use, designed, manufactured and used within a single laboratory.

Now I have just a couple of notes about enforcement discretion to sort of put

this in perspective.

We typically use, FDA typically uses enforcement discretion because of the

risks associated or how we view the risks associated with that category of tests

and in conjunction with our general resources.

But I want to note that this is not a tool that we only have used for laboratory

developed tests. In fact we've used this in many other areas where we feel that

it's appropriate.

I also want to note that enforcement discretion doesn't change the fact that the

regulations do still apply.

Now, you know, as over the years there has been an evolution in technology

for LDTs as well as how these tests have typically been marketed and the

business models that laboratories operate under.

And while there are still many tests that exist that are identical to the ones that

were under enforcement discretion back in 1976 there are also sort of these

additional tests that have what we view as an increased risk associated with

them.

And as these changes have been in occurring through technology in the

technology and business models there have been - it's been made making it a

more apparent that there are gaps in certain areas with the oversight of these tests.

Now the consequences are that there have been in some cases significant adverse health events associated with incorrect results from these tests which have led to unnecessary health care costs.

And I think the concern is that from the community that this could actually undermine the progress that's been made in all of diagnostics but particularly in the area of personalized medicine which really does depend on tests that work well.

Now it's not - this is not just an issue that FDA has been concerned with. In fact in over the years there have been several groups that have outlined concerns that they've had over this lack of regulatory oversight for laboratory developed tests.

Specifically in the 90s the National Human Genome Research Institute had raised concerns. There were two secretary advisory committees that raised concerns about this in 2000 and 2008. And then also the Institute of Medicine raised concerns about laboratory developed tests in 2012.

To address these concerns FDA actually has tried to take a number of different approaches over the years through the analyte specific agent rule and also guidance documents associated with that and then also through a draft guidance document called IVDMIAs which was published in 2005 and 2006.

Through these efforts we've have heard from stakeholders that really we need to take a more overarching approach to give better clarity to the community

Page 6

all about where we're headed with in terms of oversight for laboratory

developed tests so that they can plan appropriately.

To sort of kick that idea off in 2010 we actually did hold a public meeting to

discuss these issues. If we were to have an overarching framework for LDTs

what should this framework look like?

And the intention of the 2010 public meeting was really to gather input and

concerns from stakeholders as we are moving forward in this process.

Now that public meeting was incredibly well attended. We had actually over

600 people participating on site and a couple hundred additional folks

participating via Webinar.

We got a lot of feedback at the meeting and then actually in the public docket

following the meeting. And all of that feedback was considered as we were

moving toward drafting this framework document.

So because of that framework really or that feedback was really essential to

how we began our process for drafting the draft guidance document I wanted

to spend just a couple of minutes talking about what we did hear from

stakeholders.

So specifically we heard that no matter how we proceeded it should be using a

process that allows for stakeholder input and that can leverage external expert

opinion on this topic.

Almost every participant noted that we should use a risk-based strategy and

that it would likely be appropriate to phase in that strategy over time to allow

for greater planning on the part of labs, that we should provide some sort of a

reasonable transition period so that laboratories can sort of get up to speed without really impacting their operations too much.

And that we should provide a clear definition of laboratory developed tests so that folks really understood where - which tests this applied to.

Further a lot of folks noted that we should have a registry, some sort of way of collecting information on tests and that we may want to partner with other agencies in order to get at this information.

And then finally that there needed to be sort of a process to address situations in which rapid developments of tests were needed for example in emerging diseases or emergency situations.

Now additionally stakeholders noted that there may be certain areas where less oversight may be appropriate, particularly in the situation with rare diseases, situations where there is no other FDA approved or cleared alternative, in settings where there may be greater oversight by or greater interactions among the pathologist and physician that could help facilitate appropriate test interpretation and use such as with a hospital-based test, tests that have a really extensive peer review, established peer review and then level of evidence associated with them as well as tests that are performed in certain types of accredited labs or that have already received some sort of approval from New York State.

We also heard from stakeholders that post-market surveillance or MDR or adverse events reporting was important and needed to protect public health and that in any case no matter how we proceeded laboratories would likely need significant education on this oversight process.

So that sort of leads into, you know, how we drafted or we developed the draft proposal which was published earlier this month.

Now what we have proposed is that there will be certain categories of tests that are outside the scope of this framework and essentially that would remain under enforcement discretion for all categories of requirements.

These specific categories of tests include any test that's used just for forensic or law enforcement purposes as well as certain tests used in high complexity histocompatibility laboratories for the purpose of transplantation.

Now all other laboratory developed tests outside of those two categories would actually be subject to some level of oversight under this framework.

Specifically all of these tests would be subject to registration and listing with an option for notification in order to collect basic information on those LDTs as well as FDA would begin to enforce adverse event reporting requirements for all of those laboratory developed tests.

Now the idea with collecting this information is actually to create a basis of understanding of these tests and how they're used and how what issues or risks may be associated with them to feed into a public process that would use advisory panels and expert opinion to both classify devices that have never been classified under FDA's current system as well as to provide recommendations to FDA on how we should prioritize our enforcement of applicable regulatory requirements on this device.

As part of that we have actually identified certain categories of tests where we would be enforcing our premarket review and quality system review

requirements within a relatively short amount of time so one year after the final guidance document was published.

And then for the remaining category of tests so the remaining LDTs that advisory panel would inform how we would enforce those priorities using a phased-in enforcement approach over approximately nine years.

I should note too that certain areas will remain or certain categories will remain under enforcement discretion for the premarket review and quality system review requirements. And I'm going to talk about those in a moment.

So one of those types of tests that will remain under enforcement discretion for premarket review and quality system review requirement is traditional LDTs.

Now how FDA will sort of evaluate whether a test is a traditional LDT or not is by the following factors.

One would be whether it's an LDT by the definition that we've put forth in this guidance document in that it's designed, manufactured and used within a clinical lab, a single lab, whether it's manufactured and used by healthcare facility labs for a patient that's being diagnosed and/or treated at the same facility or within that facility's health care system.

And just to provide you some context as to why we had included that factor, one of the areas that we have heard at the public meeting that helped mitigate the risk is good interactions and communication among the pathologists and the physician, the physician to help the pathologist understand sort of what the unique conditions may be on the part of the patient so that they could take

those into account when they were determining which test was appropriate and how to interpret that test.

And the pathologist actually being able to explain to the physician sort of any limitations or, you know, that might need to be taken into account when they are - when the physician is interpreting how to move forward clinically based upon that test result.

So, you know, by ensuring that this test be done within a healthcare system would ensure sort of common ownership as well as computer systems that could help facilitate these types of interactions.

Another factor is whether or not that device is comprised of only components and instruments that are legally marketed for clinical use.

And here what we're talking about are things like analyte specific reagents, general-purpose reagents or components or devices that have already been regulated by FDA.

So for example things like microscopes or stains which are already regulated would be included in these types of components.

And then finally whether or not the test is interpreted by a quality lab professional without the use of automated instrumentation or software for interpretation.

And the reason that we included this factor is really because we wanted to rely on sort of the expertise and training of the pathologist which is regulated under CLIA and not focused on software or instrumentation which actually may need additional review to ensure that it's working appropriately.

So another category that would remain under enforcement discretion for premarket review and quality system review requirements would be LDTs for rare diseases.

And how we define an LDT for rare diseases first whether or not it actually meets the definition of an LDT and then further whether or not that test is performed less than 4000 times per year. And that is based upon the definition in the humanitarian use device regulation.

The third category that will remain under enforcement discretion for premarket review and QS review requirements are LDTs for unmet needs.

How - the factors that we'll consider for this category of tests is again whether or not it meets the definition of an LDT, whether there is a cleared or approved IVD available for that specific intended use and again whether or not that device is performed within the same health care system under which the patient is being treated.

So I think it's easier to think about these different categories by looking at a picture so that's what we've tried to sort of put forth here.

So you can see the top two LDTs for forensic and then the LDTs that are intended for transplantation. Those are outside the scope of this framework and so we will not be enforcing any regulatory requirements on those two categories of tests.

For and then you can see below that there are other categories of tests the low risk Class I devices, traditional LDTs, rare LDTs and LDTs for unmet needs that will be subject to certain enforcement of certain requirements namely

registration and listing or this optional notification and MDR reporting requirement but will remain under enforcement discussion for premarket review and quality system review requirements.

So again I think I like pictures. I think it's helpful. So we actually - there are timelines associated with when the different requirements will actually kick in for various categories of tests.

So for all of the tests that are subject to registration and listing with the option of notification as well as MDR reporting requirements that will begin six months following final publication of this guidance document.

Now after that the highest risk classes of tests, the ones that we've already indicated we will begin to enforce our premarket review requirements on those will be subject to those requirements after one year following final publication of the guidance document.

Now any subsequent tests will actually be the exact timing for when those - we will enforce premarket review requirements will depend on sort of information and the recommendations we receive from the advisory committees.

But we're - we are estimating that we would target high risk LDTs within two and five years of the final guidance publishing and moderate risk LDTs between years five and nine following final publication of the guidance document.

So just to sort to clarify this in another way at the time the final guidance publishes if there is no existing LDT on the market they will actually need to - that comes on - so if a new LDT comes on the market that's in the highest risk

Page 13

category of tests which we've identified will be the first up for enforcement of

premarket review requirements, those before they come on the market would

actually be subject to premarket review requirements.

So they could not enter the market without making a submission and receiving

approval from the FDA.

At six months following the final publication of the guidance document we

would begin to enforce registration and listing or the optional notification and

then adverse event reporting for all currently marketed LDTs except those two

categories which we've indicated are outside the scope of this guidance

document.

I should note that after that six month time point any new LDTs that enter the

market actually should notify prior to marketing that device.

And any significant changes to the intended use of an existing LDT should

actually again re-notify before they begin offering that test to patients.

At one year I've already stated that we will begin to enforce the pre-market

requirements for those LDTs in the three categories that are first up for

enforcement of premarket review requirements.

Should note that there is a requirement that they comply with QS reg at the

time that they make the PMA submission and compliance with the registration

and listing also at the time that they make the PMA submission.

One thing I do want to note is that we will not be asking the laboratories with

these tests to remove these tests from the market while they're under review.

In fact they can remain on the market while they're under review while we're working with those laboratories to obtain approval for the devices.

The only point at which they would have to come off the market is if we go through the review process and are unable to approve them.

So if we have to actually disapprove those tests because we have found, you know, issues with the safe and - safety and effectiveness of those tests at that point they would have to come off the market. But before that point is reached they would not.

So within the two year process or within the first two years as I noted we would be collecting that information on registration and listing and notification and adverse event reporting and giving that to external advisory groups.

Those groups would be helping us to classify and prioritize the remaining high-risk LDTs and at two years we would expect to actually publish a guidance document which would give information on classification and then also provide a timeline for the how we will enforce the remaining or the regulatory requirements for the remaining high-risk LDTs.

And that's what I - so I'll just skip to the next one. So at three years the group that the advisory panel indicates would be next up for enforcement of premarket review requirements at three years they would be subject to those requirements and would need to make their regulatory submissions.

And then we would complete the - all the remaining high-risk LDTs according to that priority order by year five.

And also we will in this time period we will be getting public input from the advisory panels on how to prioritize the moderate risk LDTs.

That document would publish at year four which would indicate the order in which those moderate risk LDTs should come in for enforcement of premarket review requirements. And that - the enforcement of those requirements would occur between years five and nine.

So where are we today? Today we're actually somewhat over here well beyond before this timeline actually starts. This timeline actually is triggered by the publication of the final guidance document.

And because we are only at the draft stage we are not actually enforcing any requirements prior to that to this point.

So what's next is actually that right now we're sort of in the public comment period of the guidance document.

So we actually issued a longer than normal public period. We've allowed for 120 days to receive public comment.

We plan to have a public workshop in January. We hope that you all can participate and provide feedback to us at that point.

And our goal really is to be interactive with you folks. We - this is a very complex area and we want to be able to be working with people to refine this proposal and ensure that any oversight proposal that we have is really made in the best interest of public health.

Page 16

Beyond that public comment period what FDA typically does with guidance

documents is to analyze all of the public input that we have received and

incorporate the appropriate revisions in a final guidance document.

And that publication of the final guidance document would take some time

given the fact that we do have to go through this process of incorporating that

public input and considering that public input into the final version.

Only at the point that we publish the final guidance document would we begin

to implement what's outlined in this framework.

So, you know, I think we've received some questions about okay so what can

I comment on? And really anything in the draft guidance document is up for

comment and discussion.

And I've provided sort of - there have been specific areas that FDA has asked

stakeholders to comment on. And you can find a list of those in the Notice of

Availability or the FR Notice which I think is less familiar to some people.

But we've tried to make it a little more accessible by putting it on our Web

site at www.fda.gov/ldt. And you can find a list of the specific questions FDA

would like stakeholder input on.

And I'm going to go through those as well. But even if people have questions

or comments that are beyond the scope of those items that we've identified on

this Web site we want to hear about it. And we hope that you would provide

those comments to us.

Specific things that FDA has already identified that we would like some comment and assistance from the community is particularly in the categories that will remain under enforcement discretion

So the first category of traditional LDTs in general we would like comments about whether or not these risk mitigations that we've identified here are sufficient or whether there may be additional risk mitigations that we should consider for this category of tests or additionally whether or not this category of tests should be subject to or should be subject to enforcement discretion with respect to registration and listing as well.

Now LDTs for rare diseases, one of the questions that we would hope that people would comment on is specifically whether or not the factors that are outlined are appropriate?

So is it necessary that these LDTs that actually meet the definition of an LDT and then also is the number 4000 per year appropriate or should there be another way to define what an LDT for rare disease is?

Now LDTs for unmet needs specifically the - one of the things that we struggled with when we were drafting the guidance document was how to appropriately balance the need to have patient access to tests especially in areas where there is no FDA cleared or approved alternative while mitigating the risks associated with it.

What we have proposed here is to use this to restrict the use of that to this health care facility or the healthcare system under which the lab and the patient are being treated.

So that has been our proposal. We would like input on from folks on whether or not we should define the healthcare system differently or whether there are other factors that we could consider for mitigating the risks associated with LDTs for unmet needs while still allowing patient access to these tests.

Some other things that could be clarified in these guidance documents which we've already begun to hear from stakeholders that people could comment on are how to interpret, you know, how to interpret what elements make up a medical device, what might constitute the label or labeling for a device, whether or not UDI, the Unique Device Identification requirements apply to LDTs and how laboratory physician communication about a test and its result would be viewed by FDA.

Now if you'd like to make a comment on the guidance document today I focused mostly on the draft, the overarching framework guidance document but there were actually two guidance documents that were published.

The other one was called the notification and MDR Draft Guidance document. Each of these documents have a specific docket associated with it which is listed here that you can submit comments to.

If you have any questions we do have an FDA mailbox available so you can send questions to that mailbox. Again this is not the appropriate place to make actual comments on the guidance documents.

We're hoping that the questions in here that would be submitted to this mailbox would be more clarification in nature so that you can make more appropriate comments on to the actual public docket. But we wanted to mention that this was available.

And then also we will be making this slide presentation and transcript and Webinar recording available at the following site.

And we're estimating that this would be available by no later than next Friday. And so thank you very much for your attention and we can now move toward the question and answer portion of this Webinar.

Coordinator:

Thank you. I would like to remind all audio participants if you have a question please press Star 1 and state your name clearly when prompt. One moment please for our first question. Once again please press Star 1 for your question.

First question comes from Amy Miller.

Amy Miller: Hi. Thank you very much...

Katherine Serrano: Your

((Crosstalk))

Amy Miller: ....for the overview. It was very helpful. My question is can we expect to see a

second draft of these guidance documents before finalization?

And I ask because as a coalition we've heard a variety of different suggestions

for additions to them.

And I think it would be helpful if a second draft went out for public comment

before finalization. Is that FDA's intent currently or is that open?

Katherine Serrano: Thanks Amy. That's a good question. Actually typically with guidance documents the way that we determine whether or not a second draft is needed

Page 20

is how significant the revisions are going to be, in response to the comments

that we've gotten on the public docket.

I think at this point it's a little tough to say whether or not we would have a

second draft or not. But again if the revisions are significant then we do

typically do a second round of drafts.

And the only other thing that I want to mention is that emphasizes when you

please, when you ask your question if you could please state both your name

but also your affiliation. I think it will help us provide some context for that

question as well.

Amy Miller:

Thank you, Personalized Medicine Coalition.

Katherine Serrano:

Thank you.

Coordinator:

Our next question comes from Christine Yang. Your line is open.

Christine Yang:

Hi. This is Christina Yang from Beckman Coulter. I wonder what could you

please help to understand what kind of impact to medical tax or user fees?

Katherine Serrano:

So I think the impact to medical tests I think from FDA's perspective there

would not be an impact.

This is what FDA focuses more on is the actual evaluation of the test itself on

how it performs and as well the quality systems associated with it. And we do

not focus typically on the personnel associated with running a test. That's

typically more evaluated under CLIA and so I hope that's helpful.

Christine Yang: I'm sorry maybe I didn't ask it clearly. I'm talking about a 2.3% medical tax

and also, you know, user fee and MDUFA IV in the future?

Katherine Serrano: Oh okay the medical device tax. You know, that's actually how the

medical device tax is implemented and who it applies to is actually not under

FDA's purview. It's under the IRS's purview so unfortunately I can't actually

answer that question today.

Coordinator: Our next question comes from Mr. (Binekki). Your line's open.

(Mike Binekki): Hi. This is (Mike Binekki) from GSK. I had a question with regard to let's say

tests in the guidance that fall within the gaps.

It's my - like for example a companion diagnostic tests for a rare disease

orphan drug indication versus a LDT that is used to diagnose a rare disease or

a unmet medical condition that's used as a primary study inclusion for a

therapeutic trial, so essentially a companion diagnostic test for a very rare

disease.

Liz Mansfield: Hi. This is Liz Mansfield. I'll be taking this question. Hi Mike. I think the

answer to this is the companion diagnostic requirements would trump the

LDT guidance in that case.

We have been working on how we would work to approve the guidance for - I

mean approve a device for a rare disease that was a companion diagnostic.

And we'll be addressing that in a separate forum.

(Mike Binekki): Thank you very much.

Coordinator: Our next question comes from Naomi Aronson.

Naomi Aronson: Yes Naomi Aronson, Blue Cross and Blue Shield Association. I'm interested to understand how you are defining the reporting of adverse events since in large the significant adverse events of a test are misdiagnosis. And that gets us into the area of performance. So how are you planning to define this for reporting purposes?

Katherine Serrano:

So the current MDR regulations actually specify that it includes both actual death, serious injury or a malfunction that could have led to death or serious injury.

So in the case of LDTs it would be the same. I think of course with IVDs in general I think it's harder to identify in some cases, cases where actual incorrect results have led to a patient harm or could have led to a patient harm.

But where a laboratory would identify or a manufacture of an IVD would actually identify that those events were occurring in those cases we would be expecting that they report those tests.

And I think one thing that I wanted to mention I think there's some misconceptions that FDA would be asking laboratories to sort of go out fishing or doing something different to identify cases in which their tests would be causing harm.

In fact that's not how our MDR regulations work. We - it's more of a passive system where the manufacturers when they receive reports that their devices had some sort of issue it has either led to death, injury or could have led to death or injury. Then they have systems in place to report those events to the FDA.

But they are not typically required to have systems where they're actively going out and looking for those issues. I hope that's helpful.

Naomi Aronson: Thank you.

Coordinator: Our next question comes from (Martha Ritlittle).

(Martha Riddle): Yes. This is (Martha Riddle) with (Natomics). My question is regarding just a gap I wasn't clear on the little clarification.

For a currently marketed high risk LDT that is not equivalent to any currently approved Class III device is PMA approval required or PMA submission required at that 12 month time period from the issuance of the final guidance?

Katherine Serrano: It would be a submission. So I think that's actually a very important point because as you know the preapproval between the time that you make a preapproval submission and hopefully receive approval there might be a time lag there.

And I we wanted to make sure that there was - we were being as minimally, you know, invasive as possible for those tests that were already out there.

So we actually we would be enforcing the fact that these tests make a submission at the 12 month point after the final guidance is published and they would remain - they could remain on the market through that submission process until and as soon as they receive approval, you know, they would be good to go.

Only in the cases where they actually receive a disapproval would they have to bring their device off the market.

(Martha Riddle): Okay thank you very much.

Coordinator: Our next question comes from Tom Novicki.

Tom Novicki: Yes Tom Novicki from Marshfield Clinic in Wisconsin. So regarding the

PMA and 510(k) processes, so my understanding -- I haven't done any myself my understanding -- is they are very resource intensive and can be even a

challenge for commercial manufacturers.

So I'm wondering I have several questions. First of all, will clinical efficacy need to be included clinical efficacy studies?

The second thing I'm curious about is if you have any data on the actual ability of individual hospital laboratories to really practically be able to follow this rule?

And thirdly is my personal suspicion is that this is in effect going to force many LDTs off the market because the hospital laboratories will not have the resources to really comply with the FDA rule. Thoughts?

Alberto Gutierrez: Yes hello. This is Alberto Gutierrez. So the bar for FDA approval or clearance is clinical validity, not clinical utility.

So the type of information that we ask for is to make sure that your tests have some clinical relevance.

That bar is actually not and typically believed to be that the agency requires, you know, a controlled trials to be able to get information.

Page 25

That bar actually is not that. We believe that most of the tests that are being

provided to patients should have clinical validity.

And in all cases even though CLIA doesn't require it most people think that

they're providing a - actually clinically valid test and we believe patients

actually believe they're getting clinically valid test.

So it is that data that we think needs to be reviewed by a third-party and that

needs to be assessed for, you know, whether the test actually works or not.

Whether they will be, whether laboratories will be - we do actually think that

laboratories will be able to submit.

We actually have many cases where small companies have come through

clearly through the 510(k) process but also through the PMA process.

And so we actually believe that it is a process that can be done and that will

result in submissions and good tests.

We don't - the purpose for doing this is not to actually prevent laboratories

from developing their tests. It is really just to assure that the tests are being

developed and provided are clinically significant and then - and appropriate

and the patient's actually protected.

We actually have a - the center particularly has always been one that has

helped small manufacturers. And we expect that the same type of help we'll

give to laboratories and we'll be able to help them go through the system.

Tom Novicki:

Okay thank you.

Liz Mansfield:

Let me add a little bit. This is Liz Mansfield. I want to make sure that people understand that where clinical validity has been well-established in the literature we can also accept peer-reviewed published literature, clinical practice guidelines and so on as part of or all of the evidence for clinical validity for tests.

So there is no need in many cases to regenerate this clinical data.

Coordinator: Our next question comes from Ms. (Kumidi Data). Your line is open.

(Kumidi Data): My question has already been asked, replied by the speaker. Thank you.

Coordinator: Our next question comes from Mr. (Matt Loft). Your line is open.

(Matt Loft): I think there is something like 11,000 CLIA labs in the United States. This seems like it's going to be a massive increase in the workload of the FDA which is already very heavily worked.

I'm wondering if you projected the cost of running this program and what that is likely to translate into in terms of user fees?

Katherine Serrano: Well so we actually the reason that we had taken, part of the reason that we had taken a phased-in approach was actually to be able to address the scope of the laboratory developed test using the resources that we do currently

have.

I know that you had mentioned that there are 11,000 I believe high complexity CLIA laboratories. Or, you know, I think it's something important to note that not all 11,000 would actually be necessarily manufacturing laboratory developed tests.

We've tried to do analysis of how many laboratory developed tests are out there in a couple of different ways and both ways that we have, you know, actually done that analysis that we have - we believe we can actually handle using the - this phased-in approach.

With respect to user fees I wanted to point out too that under the current agreement that we have with industry we would actually not be enforcing user fee requirements on laboratory developed tests.

I think whether or not laboratory developed tests would be subject to user fees is a topic for discussion in future negotiations.

Coordinator: Our next question comes from Mr. (Philip Novalisly).

(Philip Novalisly): This is (Philip Novalisly) from (Repulse Diagnostic) Solutions. My question pertains to what subtle differences are between LDTs and ASRs and multivariate assays?

Now said in a different way would a lab be able to use ASRs or even RUOs in the development and manufacture of LDTs?

Katherine Serrano: Right. So an ASR, an Analyte Specific Reagent is considered a component, probably a key component of a test which may be a laboratory developed test.

Typically research use only components because the intention of them is really to be used for research purposes.

Page 28

A laboratory could include those as a component of a laboratory developed

test but they may need to address sort of the quality of that component in

some way.

But yes it's possible that those could be incorporated as a component of a

laboratory developed test.

Now IVDMIAs is a little bit different. That's typically more of a software

algorithm that incorporates the values for many different laboratory tests and

generates a result.

That to us is considered to be a software. It's part of a medical device. And so

that would be considered part of a - also a component of a laboratory

developed test.

Coordinator:

Our next question comes from Dr. (Morazami).

Dr. (Morazami): Hello. Thank you very much for a very interesting presentation. My question

goes to regarding again the laboratory tests developed on mass spec in

hospital setting such as vitamin D or pain management.

So how FDA views that type of test with regards to regulations?

Katherine Serrano:

So a test let's say using mass spec to measure something like vitamin D in

a hospital situation I think we would because you're using that information to

inform a clinical decision we would consider that to be a test. And it could be

considered to be a laboratory developed test. So it would be subject to...

Dr. (Morazami): No I...

Katherine Serrano: ...the framework as one - a laboratory developed test.

Dr. (Morazami): Right. However pain management as well that basically those drugs are

measured in the urine for compliance monitoring.

So those are also considered as a laboratory developed test. But how this

document address those tests?

Katherine Serrano: So I think it's, the advisory panel those would be considered to be laboratory

developed tests subject to the proposal in this framework.

Those specific tests are not called out in the highest risk category of tests. And

so they will - the advisory panel will determine sort of at what time period we

would actually enforce the pre-market review requirements.

You should note vitamin D for example is a Class 2 device so that would be in

that moderate category which would be addressed sometime between years

five and nine.

Dr. (Morazami): Oh okay. Thank you so much.

Katherine Serrano:

Sure.

Coordinator:

Our next question comes from Ms. Katya Ms. Ledin. Your line is open.

Dr. Katya Ledin: Hi. This is Dr. Katya Ledin with Napa-Solano-Yolo and County Public Health

Laboratory.

Page 30

And my question was whether public health laboratories are considered to be

inside or outside the scope of this framework and if anybody has asked about

that previously?

Katherine Serrano:

Sure thank you. No we do consider public laboratory or public health

laboratories to be inside the scope of this framework.

I should note we have a history of working with the CDC on tests that have

been distributed out through the public health laboratories and for emerging

diseases for example, things that require emergency use authorizations.

We've already been using the emergency use authorization process to actually

ensure the quality of those tests and their performance.

So I think we have established, you know, a process for that anything beyond

that would still be under the scope of this guidance document.

Dr. Katya Ledin: Okay so we're hoping to provide some input because their public health

laboratories are really not mentioned within any part of the document. They

seem to be, you know, kind of missing so it doesn't - we're curious about how

they fit into the framework...

Katherine Serrano

Great Well

((Crosstalk))

Dr. Katya Ledin: ...in the front level.

Katherine Serrano: ...I think we'd be as with any group we'd be happy to talk with you at least

if you have specific concerns.

Dr. Katya Ledin: Thank you very much.

Coordinator: Our next question comes from Mr. (Steve Corvaira). Your line is open sir.

(Steve Barberra): Yes hi, (Steve Barberra) with (Specific S). Thanks for putting this together. It's been very helpful.

I think my question may have been answered but I'll put it out there.

A lot of us that have products out on the market currently and that are seeking coverage through the payer and so forth are putting data together.

It said in the draft proposal that existing data could be submitted and considered for the PMA process which you pointed out with clinical validity to be available.

If a company were to proactively ahead of the curve submit that data but kind of not understanding what exactly would be required and that data was not supported would that be an official denial of premarket approval or would there be an opportunity to augment that data so you could stay on the market? As you can imagine that would be pretty critical.

Katherine Serrano: Right. I think - I mean I think it depends what's going on. What I would recommend is for your - to anybody in this situation I would recommend that you come in.

We have a mechanism called a pre-submission where we can actually interact on what it is that you're trying to do with your device and how and ask us specific questions on the data that you're trying to generate or the data that

you have, you know, and whether or not there is additional data or information that we may need to support approval.

That's actually a really great way to get feedback without having to make a formal regulatory submission. That's open to anyone that wants to use that process and including folks in this group.

So I think the best way to do that is there is information on our FDA Web site about the pre-submission process. And certainly you can email that LDT framework if you have specific questions on how to do that and we can get you set up with the right information.

Liz Mansfield: And if you'd like to find...

(Steve Barberra): (Unintelligible).

((Crosstalk))

Liz Mansfield: ...guidance on that topic you - the simplest way to find the guidance is to

Google Pre-submission and FDA and it should be the first document that

shows up.

(Steve Barberra): That's very helpful. Thank you so much.

Coordinator: Our next question comes from Ginger Wooster. Your line's open.

Ginger Wooster: Thank you. This is Ginger Wooster with Orchard Software. Currently

laboratory information systems which manage orders and results from the lab

and are external to medical devices are considered Class I exempt. Do you

have plans to make any changes for the LIS with respect to LDTs?

Katherine Serrano: That is not in the scope of sort of what we've considered in this guidance

document. And I think I just want to reemphasize that anything that is Class 1

under this framework would not be subject to enforcement discretion for

premarket review requirements.

Ginger Wooster: Thank you.

Coordinator: Our next question comes from Mr. McGoohan.

Scott McGoohan: Hi. Thank you very much. This is Scott McGoohan with ACLA and I actually

had a couple of questions that I wanted to raise number one being that earlier

in your presentation you had stated that there were a number of examples of

direct harm that had come as a result of laboratory developed tests.

And I was wondering whether or not you would be able to provide examples.

I also believe that Hill had asked that that information be made available to

the community during the September 9 hearing in front of the House Energy

and Commerce Health Subcommittee. So if you could speak to that that would

be terrific

Secondly with regards to quality systems regulation requirements in that Dr.

Shuren has stated that the agency has no intent to release that third guidance

document which was discussed back in 2010 whether or not laboratories

would have an opportunity to comment on anything prior to them being

subject to that regulation.

Because under the current framework for laboratories upon submission of a

PMA which could begin as soon as 12 months after the finalization of the

guidance they would be required to follow through and abide by QSR

requirements. But there isn't a clear explanation of how those would apply in a laboratory setting.

And then thirdly getting to that user fee negotiation that was mentioned earlier, you stated that the user fees could be renegotiated going forward in the subsequent UFA.

But in that we have three years until the next UFA would take over and there's a 2% limitation on waiver authority meaning that laboratory developed tests cannot be charged user fees and the agency can only waive 2% percent of the preceding year's total user fee haul.

How do you view that as limiting the agency to carry out the tasks that they're laying out in this rather broad document?

Katherine Serrano: Sure so I'll address the first one which is about examples. I think we have provided Dr. Shuren in his testimony and in other discussions that we've had about this topic we have provided examples.

We have a number, one of the ones that Dr. Shuren actually the commissioner talked about is OvaSure is a test that it was a IVDMIA that where women were actually in some cases it was telling them whether they're at risk of developing ovarian cancer. And some women we knew had actually gone out and had hysterectomies as a result of that test when it may or may not have been correct.

There is a case of at Dartmouth where there was a whooping cough outbreak that was likely not an outbreak but it had been in - a lot of people had received antibiotics and were subject to additional testing because of results from an LDT.

There have been a number of things written in the New York Times about vitamin D testing, et cetera. You know, I think we have - we are preparing a response to - a formal response to the Hill and to the request that we've been asked to make for the Hill.

Some - I'll be frank, some of the information that FDA has is not public because of the nature of our work and so we can't share it publicly.

And also, you know, we are limited by the fact that we have not been able to systematically collect information about adverse event reporting because of enforcement discretion.

So, you know, even with all of that we have received a significant number of information from various sources about situations.

And certainly it's not just FDA that thinks, you know, that has this opinion that there have been harm. Certainly there have been, you know, external articles written about this. There were several advisory panel committees as I had mentioned that had noted these issues that made recommendations to the FDA based on those issues so I just wanted to point that out.

But certainly I think the examples that we do have we are looking for a way to share them with the public.

With respect to QS reg, you know, it's a tricky area. On the one hand the regulations are already written to be very broad and applicable to a very, very broad audience in both in terms of what types of devices are subject to them as well as what types of operations are subject to them.

And what I mean by that is they are meant to encompass anything from a guy that's making something in his garage all the way up to a very sophisticated large multinational company that is making medical devices.

So they are written and with some devices as simple as a toothbrush all the way up to something very complex like an LVAD.

So I mean certainly they're very broad. When you're talking about something that's so broad giving really specific feedback on how an individual lab could actually implement that system in the context of what they're already currently doing I think it's just really difficult.

Because among laboratories you will have a very wide variety of how each of you actually implements for example the CLIA regulations or any accreditation regulations that you may have.

So I think that was the, you know, that's part of the issue. With that said what we agree that there needs to be help by FDA and other organizations to labs to help them figure out how these regulations can actually be met using a lot of the processes and procedures that they already have in place.

And we're actually working toward getting you more specific materials, educational and outreach materials that can help you with that. So there will be an opportunity for people to get access to that type of information.

Now finally the last question you have with respect to user fees certainly the -anybody can guess and, you know, postulate on what will happen in those negotiations.

In fact every time we go through these negotiation processes, it's sort of a mystery what happens. But so I can't comment on what will happen three years from now.

I can tell you in the immediate terms as I mentioned we're not actually at the stage where we're even talking about implementing these guidance documents.

We're at the draft stage. We're collecting comments. We're collecting information from the stakeholder community to move towards a final guidance document.

And because of that I can't postulate how many LDTs will actually be required to come in under the framework in the next three years.

But I think right now the better focus is to make comments so that we can all work toward a more appropriate oversight framework that we can live under.

Coordinator: Our next question comes from Mr. (Steven Day). Your line is open.

(Steven Day): Hi. This is (Steven Day) and I'm unaffiliated. As you pointed out earlier it's CLIA that regulates the personnel requirements for testing and laboratories however it's the FDA that assigns the CLIA complexity level for those tests.

It's the same framework that's currently used to assign those to manufacturer's tests, commercial manufacturer's tests going to be used to assign CLIA complexity levels to the LDTs as they go through this framework?

Katherine Serrano:

That's correct. That would be the same system. I mean I think the only thing that I noted right now LDTs are actually subject to the highest level of complexity because of the nature of being a laboratory developed test and so there is actually, you know, going through the FDA process there is a way that laboratories may actually be able to have a lower complexity test instead of that highest level of complexity.

Coordinator:

Our next question comes from (Megan Gordonson). Your line is open.

(Megan Gordonson): Thank you. And thank you for putting this together. So my question is about genetic profile panels.

So the way that I understand the guidance is that LDTs are proved for certain conditions. But how will that apply to genetic profile panels for use in determining which kind of clinical trial or off label use of drugs might be open to patients based on genetic mutations?

For example if a test for RAS has already been approved by the time this guidance goes into effect would a potential panel not be able to include a RAS test or would that still be open on the panel?

Liz Mansfield:

So that's a very good question and one that we have put a lot of thought towards and that is not addressed in the guidance. This is Liz Mansfield by the way.

What our current belief is is that if a panel contains a marker that is approved as a companion diagnostics we would consider at least that marker to be a companion diagnostic.

If the panel includes other markers that are not related to the use of that companion diagnostic it's unclear exactly how we would handle that right now and we would love to hear your comments in the comment period about how we should handle that.

(Megan Gordonson): I appreciate that. Thank you.

Coordinator: Our next question comes from (Jerry) Hearn. Ms. Hearn your line's open.

Sherry Hearn: Hi. This is Sherry H

Hi. This is Sherry Hearn I'm calling from the Oregon State Public Health Lab. I was hoping to get some more information about how this guidance is going to apply in the circumstance of screening tests, in particular newborn screening tests that are frequently done on hundreds of thousands of children and if because it's a screening test and not a confirmatory test if this guidance would apply?

I was also interested in getting more information about how the test for rare diseases would apply in the cases of outbreak situations where you might normally only perform ten or 20 of a particular test in a year but during an outbreak situation you might be asked to do several thousand and how the FDA would address those situations and the changing needs of state public health labs?

Katherine Serrano: Okay. So I'll address the first question first about things like the screening tests.

Those would be considered LDTs that would be subject to this framework. And I think again it would be up to sort of that advisory panel to determine what the relative risk was and where they should fall in terms of when we

would begin to enforce the premarket review requirements on those that have actually not that don't have an FDA approved equivalent.

Now with respect to rare disease testing this is actually an area that we again as Liz noted we have provided we hadn't thought a lot of that out. But we haven't addressed that issue that you mentioned where the outbreak situation.

We may have a mechanism already to deal with this which could be the existing emergency use authorization mechanism.

But again if you have additional ideas on how we could address the specific issue of rare diseases and how we might need to modify that definition to address some of these issues we would love to hear that in the comments.

Sherry Hearn: Okay thank you.

Coordinator: Our next question comes from Christine Gathers.

Christine Gathers: Hi. This is Christine Gathers from Eli Lilly and Company. We have a clarification question regarding the guidance scope and wanted to verify that it's directed just to commercial LDTs or does the guidance also apply to LDTs used for R&D purposes? Thank you.

Katherine Serrano: So the guidance would only apply to those LDTs that are being used for clinical use. So if you're using them for R&D purposes you're not - and I'll be more specific, purposes where you're not actually reporting that result back to the patient or that don't meet the definition of a significant risk device requiring other actions under our regulations then those would be outside the scope of this guidance.

But if you're actually performing those tests on patients or - and giving them the result or that you meet the definition of a significant risk device even during your R&D purposes those would be subject to this guidance.

Christine Gathers: Thank you.

Coordinator: The next question comes from (Art Komasaki).

(Art Kawasaki): Hello. (Art Kawasaki) Care of Cannon US Life Sciences. I had a follow-up scope clarification question that is aligned with the question that was just

asked and one prior regarding RUO components.

I wanted to know if there's an impact if any to the manufacture of an RUO labeled instrument system that is used by a lab to develop an LDT for patient management or treatment decisions?

Katherine Serrano: I think that those responsibilities would be the same that they already are so this wouldn't impact those responsibilities.

(Art Kawasaki): Okay thank you.

Coordinator: Our next question comes from Pat Smith.

Pat Smith: Yes hi. Thank you very much for today. This is Pat Smith Lyme Disease Association. And I have two quick questions.

One concerns the expert panels that you, the advisory panels that you intend to convene. I would like to know how those panel members will be selected, what the criteria would be, and particularly how would they be screened for conflicts of interest? That's question number one.

And question number two is those individuals or entities who have expressed opinions that existing tests are harmful I'd like to find out if their comments were considered in light of any conflicts of interest they may have had? Thank you.

Katherine Serrano:

Thank you for those questions. So with respect to the panels and the advisory panels that we would use typically what I can say what we have done in the past when we've had panel meetings -- and FDA has panel meetings at some frequency -- we did this when in - after the initial 1976 medical device amendments were passed to actually classify devices.

And we continue to have panel meetings when we're making very, you know, decisions that are controversial or that can really impact the respective field.

We have a lot of rules for how those panels are made up from who is on them that typically include a wide variety of experts in that field and different stakeholders.

So for example patients, patient groups are represented on those panels as well. And there is an extensive screening process for conflicts of interest for - the members of those panels and specifically the types of issues that they are, you know, asked to address in their panel meeting.

Now with respect to the how FDA has evaluated the situations where we've heard of harm, we have carefully evaluated all of the evidence including the source of the evidence.

Some of the time that's why it is difficult for us to actually give public information out about, you know, what exactly we have heard because

sometimes the sources - because of the sources we are not actually able to share that information.

So I - we have considered all of that information when we're making these evaluations.

Alberto Gutierrez: This is Alberto Gutierrez. I wanted to add so that it is understood the panels that we'll be putting together will only (delve) onto the risk of the devices and when they have to come in.

There may be cases when we have devices that are going through the process, the approval or clearance process.

But there are cases where we actually take those devices to panels themselves.

And so that may be also a time when a panel will be put together and what will be a chance to have public comment and actually the process of determining whether the device is safe and effective is open to a broader discussion by stakeholders.

Coordinator: Our next question comes from Angela Tucker, Roche.

Angela Tucker: Hello everyone good afternoon. Thank you for putting on the Webinar. This is

Angela Tucker with Roche Molecular.

My question goes to Dr. Gutierrez. Dr. Gutierrez you mentioned that the bar for LDTs is clinical validity not clinical utility.

My question to you is will this also shape or inform the requirements for clinical utility demonstrations by IVD manufacturers? Thank you.

Alberto Guiterrez: So the bar of clinical validity actually is the one that we use for all IVDs. We

don't actually look at clinical utility we look at clinical validity.

Angela Tucker: Thank you.

Coordinator: Our next question comes from Mary Williams. Ms. (Williams), your line is

open.

Mary Williams: Hello. Thank you, Association for Molecular Pathology. This isn't the only

guidance that will - that laboratories need to follow to understand what

requirements are associated with this oversight.

Will there be a catalog or library where laboratories can find all of the other

guidance documents for example for companion diagnostics and a variety of

guidances for industry that have that are in existence?

Katherine Serrano: Yes. We have a Web site where all of our guidance documents are

published. I think you're asking for something a little bit more specific

somewhere where that they can more easily, you know, get to the ones that are

specifically applicable to laboratories.

And I think that certainly that's something that, you know, please submit that

in a formal comment. I think that's definitely something that we could easily

do.

Coordinator: Our next question comes from Richard Robinson.

Richard Robinson: Hi. Richard Robinson from the American Red Cross. My concern is with

respect to the serological test LDTs done to determine red cell compatibility

which were specifically called out as being among the top tier for enforcement under the new guidance.

I wonder if you could - I have several questions. I wonder if you could clarify how - well let me back up.

There are a number of laboratory developed tests that are described in peer review copyrighted journals, serological tests for determining red cell compatibility in situations where there's no commercial kit available.

And I'm a little unclear how any one particular lab could submit a premarket authorization for a serological test that's described in a peer reviewed journal.

And if they did, you know, these tests are widely used in reference and blood bank reference labs. Would each laboratory be required to submit a premarket authorization for each of those tests?

Third question is even if the user fee was waived for the premarket submission there is still a user fee associated with the device establishment registration correct?

And a fourth question, last question is even in the event, even with the best, all of the testing that goes on, you know, patients still react to red cell transfusions.

Wouldn't some sort of a red cell transfusion reaction trigger a medical device report it each time it happens?

Katherine Serrano: So unfortunately we don't have our CBER colleagues here. They are the experts on this - these particular set of questions.

Page 46

The one that you - so I would actually encourage you to submit your specific

question to the LDT framework...

Richard Robinson:

Sure. That's fine.

Katherine Serrano:

...email that you - that I have provided. And I can actually get you the best

answer to that as possible.

Regarding the user fee question that you have right now under the current

MDUFA that the fact that user fees are not collected applies to any user fee

and the device establishment registration that's part of the registration listing

fee and that actually is included in that.

So that at this point under this MDUFA agreement they - we would not be

collecting user fees for that.

Additionally you'll note that we actually have provided an alternative to

formal registration and listing for all of the laboratory developed tests that

aren't actively being regulated for premarket review and quality system

regulation requirements.

That notification we actually created that as an alternative because we wanted

to kind of get around the user fee issue for tests that weren't actively being

regulated so that we would have a mechanism for getting at, you know, what

was being offered and getting that information to feed into the advisory panel

process and also to be a resource to the community to know what tests are

actually being offered but without having to trigger that notification or that

registration and listing fee that would be associated with that.

Liz Mansfield:

And regarding the - I'm sorry Liz Mansfield regarding the MDR reporting, we are aware that no test is perfect and that there will be results that could cause for example as you said red cell reactions, would that be reportable as a medical device report?

The answer is yes if you believe it caused a serious injury or death or a malfunction has the potential to cause serious injury or death.

Now reporting in medical device report does not mean that you must take your product off the market or that FDA will necessarily take any action.

It's our way of monitoring tests over time to assure that if there are systematic problems they can be addressed appropriately.

Katherine Serrano: I think that's a good point by Liz. And I think I just want to follow-up on it too. Certain types of devices we don't typically see a lot of MDRs.

And so any MDR might initiate some interest on FDA's perspective when we would reach out to the company and kind of try to figure out what was going on.

But with other devices I can tell you for example in the glucose area we receive so many MDRs for glucose meters that we don't follow-up with every single, you know, individual report that we receive.

We evaluate them, we monitor them, we looked at sort of frequencies and compare frequencies but each individual report would not be actionable.

Coordinator: Our next question comes from (Nancy Yote). Ms. (Yote) your line's open.

(Nancy Yote):

Thank you for the seminar. It's been very good. This is (Nancy Yote) from (Brenwood) Biomedical.

And my question is if a clinical lab is developed in LDT and they decide or they wish to license it to another laboratory does this move the test into the commercial IVD category requiring a 510(k) or a PMA submission?

Katherine Serrano:

Well so I mean I think under FDA's definition yes but what we have tried to do in the framework is actually a lot - we know that this goes on a lot. And because I think we felt that it was more important to sort of move forward with the framework than to get stuck in a discussion with what does or does not meet the definition of an LDT, we have stated in the guidance document is that if you're calling it an LDT regardless of whether it meets that strict definition that we've outlined in the guidance document this framework will apply.

(Nancy Yote):

Okay.

Katherine Serrano:

Now for the...

(Nancy Yote):

Okay thank you.

Katherine Serrano

: ...categories that will remain under enforcement discretion if the category has under it a factor stating that it needs to meet the definition of an LDT it does actually need to meet the strict definition to be eligible to remain under enforcement discretion.

And so in your particular case and that scenario that you had outlined they may not be able to be considered for example as an LDT for an unmet need.

(Nancy Yote): Okay.

Katherine Serrano But again those factors are under discussion. There you can certainly

comment on them in the formal process and give us your opinion as to

whether you think that is or is not an effective mitigation of risk.

(Nancy Yote):

Okay. Thank you.

Coordinator:

Our next question is (Diana Lane). Ms. (Lane) in your line is open.

(Diana Lane):

Hi. This is (Diana Lane) from (Neterra) and I have two questions. The first question is in regard to what would happen if a high risk test that currently does not have an approved alternative is on - is being marketed but then a competitor gets approval during that T0 to two year window before the prioritization guidance is published by the panel.

Would there be some sort of grace period to get a submission in because that would move the affected test up to the immediate category that was supposed to have started submissions in one year.

Katherine Serrano:

So actually the guidance does talk about this point in that especially for those tests that are in those the highest risk categories the ones that will be subject to enforcement discretion.

As you mentioned there may be a device in that time period let's say at year two that comes on the market that actually receives PMA approval.

So at that point what the guidance says for the LDTs for unmet needs that there is basically other tests on the market with that same intended use would have a year in order to make a submission a regulatory submission.

Now again they would remain on the market while that regulatory submission was being reviewed so they would have essentially a year grace period to get their documentation together and make that FDA submission and then they would have - they would be able to remain on the market until FDA issued the approval or hopefully approval and only if they receive a disapproval would they have to come off the market.

(Diana Lane):

All right, thank you for clarifying that. For my second question you mentioned during your presentation that recognition of New York State approvals had been proposed in 2010 but that suggestion didn't appear in the draft guidance at least as I read it.

So for tests that already have New York State approvals would there be any recognition of that in - of that approval in facilitating FDA approval?

Katherine Serrano:

It was a comment that we did consider. I think one of the things that we, you know, we didn't want to create a system where we were essentially passing our responsibilities off onto New York State. I think that was one of the considerations that we had in that, you know, as we were drafting guidance document.

Certainly that's an area where people can comment on it and make, you know, their recommendations.

But to answer your question I'd say under our framework we would not consider whether or not it had received New York State approval when - on whether or not they would actually have to go through the process outlined in this guidance document.

(Diana Lane): All right thank you.

Coordinator: Our next question comes from Mr. Tim Webster.

Tim Webster: Hi. Good afternoon. Thank you to the panel for the help, Tim Webster from

Webster Consulting.

So one of the things that I work with is CAP gap analysis for laboratories, two parts to the question. The first one is, is there any intention to deputize the CAP to help with this process?

And second one is the idea that some tests are currently FDA approved or cleared while competitors are not.

During this process does this mean that marketing will be able to talk about FDA approved tests once we have gone through this process? Thank you.

Katherine Serrano

So regarding the first question certainly in the guidance document we've outlined the idea that we would like to work with third-party reviewers and inspectors in order to assist FDA with our workload but also particularly for the moderate risk tests but also to allow an alternative to FDA review so that laboratories can maybe choose a third party to do their reviews or inspections that they're more familiar with.

If organizations, accreditation organizations wanted to participate in this program we would be happy for them to do so. But we can't prospectively plan for a group to take to take part in this type of activity.

Now with respect to your second question tests already can note what their status is so in their marketing materials. So if they're a Class III device they can - and they received, you know, approval of a PMA submission, they can say that they are - they have, you know, FDA approval. If they're a 510(k) device they can indicate that they have clearance.

Tim Webster: Thanks very much.

Coordinator: Our last question is from Mr. Ruta. Your line is open sir.

Dr. Martin Ruta: Yes hi. It's Martin Ruta. So I'm from CBER. And I appreciate all the effort of our colleagues at CDRH. This has been a great Web cast.

And I wanted to thank Richard Robinson for his question. And, you know, we appreciate that. We can try and clarify that. And if you would send it to the docket that would help.

Liz Mansfield: Thank you Martin for that comment. So Dr. Martin Ruta is works for the

Center for Biologic Evaluation and Research and has indicated that the question about the blood typing is a CBER question and they can help with

that and that comment should be sent to the docket with all the others.

Coordinator: At this time there are no questions in the queue.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and

thoughtful questions. Today's presentation will be available at

www.fda.gov/cdrhwebinar under the tab titled "Past Webinars and

Stakeholder Calls 2014".

A transcript of this event will also be posted but may not be available before Friday, October 31.

If you have any additional questions about this guidance please use the contact information provided at the end of the slide presentation.

As always we appreciate your feedback. Again thank you for participating and this concludes today's Webinar.

Coordinator:

Thank you. Audio participants may disconnect at this time. Thank you for joining.

**END**